

Caloric Restriction and Calcium's Effect on Bone Metabolism and Body Composition in Overweight and Obese Premenopausal Women

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Obesity results in numerous preventable deaths and comorbidities. Unfortunately, a reduction of body weight has been correlated with a reduction in bone mass, the reasons for which have not been fully elucidated. The importance of maximizing peak bone mass during premenopausal years is well known. Most studies demonstrate a positive relationship between calcium intake and bone mass. However, during caloric restriction, which is commonly used for weight loss, calcium intake has shown mixed results. Calcium from dairy sources has received additional attention, beyond its importance to bone, for its role in regulating body weight and composition. Dairy foods are perceived as high fat, and therefore, are generally minimized or avoided during caloric restriction. The current calcium intake for premenopausal women is significantly below recommendations, and even if met during caloric restriction, may not be adequate. This review underscores the need for maintaining at least adequate intake levels of calcium, if not more, during weight loss regimens to minimize potential long-term detrimental effects on bone metabolism.

Key words: weight loss, caloric restriction, calcium, bone mineral density

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Introduction

Obesity has reached epidemic proportions in the United States, with two out of every three adults classified as

obese or overweight.¹ National Health and Nutrition Examination Survey (NHANES) data show an increase in the age-adjusted prevalence of obesity from 22.9% in the years from 1988 to 1994 to 30.5% for the years from 1999 to 2000.² The prevalence of overweight individuals during the same time periods also increased from 55.9% to 64.5%. Increases in mortality attributable to obesity are approximately 280,000 per year,³ and include numerous comorbidities such as cardiovascular disease, type 2 diabetes, osteoarthritis, hypertension, certain cancers, gall bladder disease, and others.^{4–6}

Osteoporosis and related diseases are increasing. Approximately 40% of women at 50 years of age will experience an osteoporotic fracture during their lifetimes.⁷ Osteoporosis is a disease that causes low bone mass, resulting in increased susceptibility to various fractures. It has been estimated that over a women's lifetime, about one-half of her trabecular bone and one-third of her cortical bone will be lost.⁸ The prevalence of osteoporosis is expected to increase over the coming decades,⁹ and is likely to become the most common disorder in the aging population.¹⁰

Caloric restriction is a typical approach employed by individuals to reduce excess body weight. A significant proportion of the public engages in weight loss activities,¹¹ which are recommended to address the health risks associated with obesity.^{12–14} The positive effects of weight loss on chronic diseases have been well documented both in patient health and in health care costs.^{15,16}

Obese women are thought to be at decreased risk for osteoporosis because of the mechanical influence of increased load on bone mass. A reduction in body weight has been correlated with a reduction in bone mass, which could be a catalyst for future osteoporotic disease. It has not been fully elucidated whether this reduction in bone mass with weight loss is due to: 1) the weight loss itself, 2) measurement error, or 3) inadequate calcium intake. Calcium is one of the most investigated nutrients in relation to bone health. Current calcium intake in premenopausal women is well below national recommenda-

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tions. Major calcium food sources, such as dairy products, are perceived as high fat and are therefore generally minimized or avoided during caloric restriction. This could have implications for bone health. However, calcium from dairy sources has received additional attention for its role in regulating body weight and composition, particularly fat mass, and simultaneously may have a positive effect on bone health.^{17,18} This review will examine caloric restriction for reducing body weight and its effect on chronic disease and obesity, the effect of caloric restriction on bone mass, and the role of calcium in weight loss, body composition, and bone health during caloric restriction. Considerations among the various sources of calcium and the effect on other diseases will also be examined. Suggestions for intake levels and calcium sources during caloric restriction will be provided based on available studies.

Obesity and Bone Health: Relationship of Body Composition and Bone Mass

The effect of obesity on bone metabolism is not understood, but a positive relationship exists between body weight, body mass index (BMI), and bone mass or bone mineral density (BMD). This relationship has been shown for both total body bone mass and for regional sites, e.g. the spine and femur in pre-, peri-, and postmenopausal women.¹⁹⁻²⁶ Rico et al.¹⁹ assert that body weight is the chief determinant for bone mass in women. Low body weight is an independent predictor of low bone mass later in life.²⁷ Percentage of body fat in premenopausal and older women is also significantly related to total body BMD.²⁰ In older women, the percentage of body fat also correlates well with BMD.²⁸ Possible explanations for the protective effect of obesity, aside from mechanical load on bone, may be the additional conversion of estrogen from androstenedione in adipose tissue or a reduction in sex hormone binding globulin.^{23,29-32} As obesity increases, bone mineralization increases, thereby reducing the risk for osteoporotic diseases.

Many but not all³³ cross-sectional and longitudinal studies have shown bone loss in premenopausal women. When examining outcomes related to bone mass, a decrease in hip fractures as a result of greater body weight has not been demonstrated in all studies,^{28,34-36} but it is clear that osteoporotic fracture risk is higher in women with lower body weight than in heavier women.^{22,23,37} Again, however, these differences have not been found in all studies.²⁸ Interestingly, a prospective study by Johansson³⁸ found BMD to be a better predictor of death than blood pressure and cholesterol. Furthermore, low bone mass was an independent predictor of survival.

Effect of Caloric Restriction on Bone Mass

It has been established that bone density can predict future osteoporotic disease, and that low BMD is one of the strongest risk factors for hip fractures.³⁹ Low peak bone mass is also an osteoporotic risk factor.^{40,27} Many studies investigating changes in bone mass in women have suggested that bone mass begins to decrease after peak attainment in the thirties and prior to menopause.^{33,41,42} One recent six-year prospective study determined that bone loss at the femoral neck began as early as the mid-twenties.⁴³ Another study estimated that 99% of peak total body BMD occurs in women between the ages of 19.6 and 24.6 years, and 99% of total body bone mineral content (BMC) was attained between the ages of 22.5 and 29.9 years.⁴⁴

Observational studies have indicated an increased risk for hip fracture in women who experience weight loss during early or middle adulthood and later in life.^{35,36,45-48} Several studies have indicated that with weight loss there is a concomitant loss of bone mass either for the total body or for regional sites.⁴⁹⁻⁵⁷ Weight loss protocols in these studies ranged from 10 to 24 weeks in duration, with one lasting as long as 12 months.⁵⁸ Additionally, in studies examining eating behaviors of women, Van Loan et al.⁵⁹ found on average a 12% lower BMC in women with cognitive dietary restraint and normal to low body weight. Furthermore, Bacon et al.⁶⁰ found that in a group of premenopausal obese women with histories of chronic dieting behavior, one-third had either osteopenia or osteoporosis. These studies clearly demonstrate that dietary restriction is negatively associated with bone health.

Role of Calcium on Bone Mass

As one of the major minerals in the skeleton, calcium has been well researched in relation to bone growth, preservation, and health. The adult human body contains roughly 1000 to 1500 g of calcium, making it the most abundant mineral, and 99% of it is located in the bones.⁶¹ Current recommendations for women 19 to 50 years of age are 1000 mg/d.⁶² The 1994–1996 Continuing Survey of Food Intakes by Individuals (CSFII) estimated the mean intake of calcium in women 18 to 50 years of age to be approximately 640 mg/d—only 64% of the recommendation.⁶² In a more recent NHANES survey (1999–2000) calcium intake was about 770 mg/d for women 20 to 59 years of age, up slightly but still only about 75% of the recommended level of intake.⁶³ Both averages fall significantly short of current recommendations and are quite distant from the upper intake level for calcium set at 2500 mg/d.⁶² These averages also fall below a requirement of 975 mg/d determined in a premenopausal calcium balance study.⁶⁴ A NIH Consensus Conference in 1994 highlighted calcium as one of two nutrient defi-

ciencies in the United States that warrant a national effort to increase average intake levels.⁶⁵

Low calcium intake can limit bone formation in early life and cause bone loss in maturity.⁶⁶ Two epidemiological studies confirmed this finding and demonstrated an increased risk for hip fractures in women later in life.⁶⁷⁻⁶⁸ Supplemental calcium has been shown to reduce the risk of hip fractures.⁶⁹ Variations in calcium intake during youth have been estimated to affect peak bone mass by only 5% to 10%, whereas the influence of hip fracture risk later in life may account for 25% to 50% of risk.⁷⁰ While other vitamins and minerals have been looked at, calcium is clearly the most well researched.⁷¹

A meta-analysis of 33 cross-sectional, longitudinal, and intervention studies found a small but significant positive correlation between calcium intake from either supplement or diet and either BMD or BMC in women 18 to 50 years of age.⁷² Mean calcium intakes were between 436 and 1437 mg/d. A second meta-analysis using 49 investigations of early postmenopausal women examined the relationship between calcium intake and bone mass, and also found a positive correlation.⁷³ More recent studies⁷⁴⁻⁷⁶ report conflicting results. Heaney⁴⁰ performed the largest meta-analysis to date of studies using calcium supplements or diet (dairy products) and reaffirmed the positive relationship between calcium intake and bone mass. This finding was consistent in the 139 studies examined, with the exception of two randomized, controlled trials and 21 observational studies; 83% of the studies showed a positive relationship. A fourth meta-analysis by Weinsier⁷⁷ of 46 studies in which only dairy products were used achieved mixed results; the authors concluded that there was inadequate evidence to support a recommendation for daily intake of dairy foods for bone health. This report prompted an editorial discussing categorical decisions in Weinsier's meta-analysis (e.g., classifying an observational study in a strength category that included randomized, controlled trials).^{78,79} Relative to calcium supplements versus dairy foods and the impact on bone, two of the six dairy studies in the meta-analysis⁷⁸ indicated that supplement use was significantly better than intake of dairy; however, this observation was not noted. Furthermore, a clinical trial⁸⁰ and one retrospective study⁸¹ did not find a significant relationship between dairy foods and bone mass, but an association was observed between supplement use and bone mass. This finding was also noted in another review by Gueguen and Pointillart in 2000.⁸² Finally, one recent study not included in the above analyses showed a protective role of dietary calcium on bone mass by lowering the rate of bone loss in premenopausal women 25 to 30 years of age.⁸³

Overall, it appears that calcium intake has a statistically significant influence on bone accretion and bone

preservation based on the vast majority of studies. Although research suggests that other nutrients, such as vitamin D, are also important, it is calcium that has the greatest bone-preserving and bone-building effect.⁸⁴ The issue of calcium intake is of paramount importance, particularly as the median intake for females falls short of recommended levels after childhood, even when supplemental calcium intakes are included.⁸⁵

Role of Calcium on Bone Mass During Energy Restriction

Because of a demonstrated loss of bone mass during caloric restriction, and because calcium intake has been shown to increase or preserve bone mass, it has been recommended that calcium supplementation be given during weight loss regimens.⁸⁶ Calcium has been identified as one of the nutrients at risk in diets used for weight control.⁸⁷⁻⁸⁹ Studies have been conducted to determine the effect of calcium intake on bone mass during caloric restriction. Relatively few premenopausal studies have been reviewed, so postmenopausal studies will be included as well (Table 1). A caloric restriction study that randomized pre- and postmenopausal obese women to a group receiving 1 g/d of calcium or to a control group for 3 months found a significant difference between groups in whole body and spine BMC, with the calcium-supplemented group losing less BMC.⁵³ A 3-month follow-up measurement showed no change in weight in the supplemented group, but the control group had gained weight and continued to lose more BMC. The supplemented group had no change in BMC, suggesting continued bone preservation for calcium supplement use.

A 6-month caloric restriction study by Shapses et al.⁹⁰ randomized obese premenopausal women to groups receiving: 1) 1 g/d of calcium with caloric restriction, 2) placebo with caloric restriction, or 3) no calcium or caloric restriction (control). Although no significant differences were observed, the BMD of the spine tended to increase in the supplemented group, while the two other groups tended to lose BMD or BMC from the total body or lumbar spine. Additionally, markers of bone turnover were not significantly different between groups. These findings are in contrast to the above study by Jensen,⁵³ and suggest that calcium supplementation does not improve bone status during caloric restriction. It also suggests that low calcium intakes during weight loss do not result in a significant loss of bone, and that bone mass is not adversely affected by moderate weight loss. This prompted an editorial by Barker and Blumsohn,⁹¹ who, in re-analyzing the data, suggested that the overall change in lumbar spine BMD was not significantly different between the groups. In fact, in post hoc testing the only difference was seen between the calcium and control groups, indicating that there is no support for

Table 1. Obesity Caloric Restriction Studies Using Calcium (Ca)

Study	Subjects	Intervention	Duration	Outcome
Jensen 2001 ⁵³	62 pre- and postmenopausal women	1 g Ca or nothing (no placebo)	3 mos	Significant differences in whole body and spine BMC, with the treatment group losing less BMC. Follow-up 3 months post-completion showed no change in weight in the supplemented group, while the unsupplemented group gained weight. The unsupplemented group continued to lose more BMC, while the supplemented group had no change in BMC, suggesting continued bone preservation for supplement use.
Shapses 2001 ⁹⁰	38 premenopausal women	1 g Ca, placebo, or control group with no caloric restriction	6 mos	No significant differences, but spine BMD tended to increase in the supplemented group, and the other two groups tended to lose BMD and BMC from total body or spine.
Bowen 2004 ⁹²	50 men and pre- and postmenopausal women	2.4 or 0.5 g Ca	12 wks and 4 wks energy balance	The low-Ca group had a 40% increase in bone resorption (urinary deoxypyridinoline) and a significant increase in bone formation marker (serum osteocalcin) compared with the high-Ca group. There was no change in total body BMD in either group.
Radak 2004 ⁹³	74 men, premenopausal, and menopausal women	high dairy (1221 mg Ca), high Ca (1334 mg), low Ca (456 mg) with placebo	12 wks	Significant decreases in total body BMD in the placebo group and increases in femur BMD and lumbar BMC in high-Ca and high-dairy groups, respectively. Marker of bone formation (serum bone alkaline phosphatase) was significantly decreased in the high-Ca group.
Cifuentes 2004 ⁹⁴	57 postmenopausal women	1.0 or 1.8 g Ca with weight loss or weight maintenance programs	6 wks	For 1.8 g versus 1.0 g Ca: Serum markers of bone turnover only. Marker of resorption (N-telopeptide) showed no significant changes. Marker of bone formation (serum osteocalcin) showed a decrease and significantly prevented a rise in levels.
Ricci 1998 ⁵⁴	31 postmenopausal women	1 g Ca or placebo	6 mos	Decreased bone turnover and greater preservation of BMD in the supplemented group compared with the control group.

BMC = Bone mineral content; BMD = bone mineral density.

suggesting that the calcium group tended to increase lumbar BMD. Barker and Blumsohn⁹¹ also suggested that when extrapolating the change seen in lumbar BMD in the placebo group to a year, the 95% confidence interval would increase to a 3.5% loss in bone, which would be a significant loss for premenopausal women undergoing caloric restriction. This work supports earlier findings.

A recent 12-week study conducted by Bowen et al.⁹² examined bone turnover during caloric restriction in men and in pre- and postmenopausal women 20 to 65 years of age, and showed that low intakes of calcium (~500 mg/d) resulted in significant increases in bone turnover compared with the other diet group, who received approximately 1400 mg/d. However, this study did not show any significant changes in total body BMD in either group, probably because 12 weeks is too short a time period to see changes in BMD assessed with dual-energy X-ray absorptiometry. Recently, Radak et al.⁹³ conducted a 12-week, multicenter, randomized caloric restriction study in overweight and obese men and premenopausal women. Two groups had total average calcium intakes of 1334 ± 76 (high calcium) or 1221 ± 126 (high dairy), while a placebo control group averaged 458 ± 71 mg/d. Results showed significant decreases in total body BMD in the placebo group and increases in femur BMD and lumbar BMC in the high-calcium and high-dairy groups, respectively. Serum bone alkaline phosphatase significantly declined in the high calcium group.

These results suggest that, in the short term, high calcium intakes during weight loss can suppress bone turnover, and when consumed over extended periods of time may preserve bone mass. Interestingly, no decline in bone alkaline phosphatase was seen in the high-dairy group, who averaged approximately 115 mg/d less calcium than the high-calcium group; markers of bone formation and bone turnover remained unchanged. The lack of a significant change in bone markers for the high-dairy group was unexpected. Perhaps the 115 mg/d difference in calcium represents the threshold at which bone turnover is impacted during weight loss. This concurs with a recent 6-week calcium and weight loss study, which found that 1800 mg/d of calcium provided adequate intestinal absorption (348 ± 118 mg) that was approximately 56% greater than with a calcium intake of 1000 mg/d (195 ± 49 mg), based on an average estimated need of approximately 240 mg/d of calcium for postmenopausal women.⁹⁴ These two studies⁹³⁻⁹⁴ preliminarily suggest that optimal calcium intake in pre- and postmenopausal women during caloric restriction could be estimated to be at least 1300 mg/d for bone preservation.

Finally, results from short-term studies assessing

bone mass may be confounded by that fact that bone remodeling is believed to act in cycles, a phenomenon known as the “bone remodeling transient.”⁹⁵ Because calcium is a threshold nutrient, both the age at intake and the amount of intake can influence bone mass.⁹⁶ Most weight lost typically is regained, but whether a concomitant increase in bone density and content follows weight regain is uncertain.⁹⁷ One study assessing total body BMC 6 months post-completion found that subjects who had lost additional weight also lost additional bone mineral, but subjects who regained weight also regained bone mass.⁵⁰ Compston et al.⁵¹ also found that total body BMC approached initial levels when assessment was 10 months after a weight loss intervention with subsequent weight gain. However, Avenell et al.⁹⁸ did not observe a similar response when subjects regained weight. In summary, investigations of changes in BMD or BMC during weight reduction are not consistent in their findings. Long-term studies involving placebo and control groups with a post-intervention follow-up are needed to more thoroughly examine the effect of weight loss on bone metabolism. These studies should also include markers of bone turnover and should not rely solely on BMD and BMC values obtained by dual-energy X-ray absorptiometry to more accurately assess changes in bone health.

Calcium Intake as an Independent Regulator of Body Weight and Composition

There is now evidence from epidemiological, animal, and human experimental data to suggest that calcium may play a role in weight regulation, which could provide an additional reason to ensure adequate calcium intake during weight loss. Epidemiologic studies have indicated a strong inverse relationship between adiposity and calcium intake.⁹⁹ Zemel¹⁰⁰ examined NHANES III data and found that calcium intake was related to body weight. The relative risk for being in the highest quartile of adiposity was highest among those with the lowest calcium intake. This observation persisted when physical activity and energy intake were controlled. Davies et al.¹⁰¹ explored the relationship further by retrospectively analyzing five observational and cross-sectional studies of pre-, peri-, and postmenopausal women. A significant negative association between calcium intake and body weight was observed. For each age group, the odds ratio for being overweight was 2.25 for young women in the lower half of calcium intakes within their respective groups. Heaney et al.¹⁸ extended the analysis by adding an additional randomized, controlled trial to the analysis and using multiple regression analysis to predict BMI based on calcium intake and other selected macronutrients. The regression coefficient for calcium intake was significant ($p = -0.003$) and equated to the average BMI

being 0.3 kg/m² lower for each 100-mg increment in calcium intake.

Zemel¹⁰² was first aware of the relationship between calcium intake and body weight after re-analyzing a previous study that examined the effect of calcium intake on hypertension in obese African Americans. Increases in dietary calcium ranged from approximately 400 to 1000 mg/d and continued for a year, resulting in a 4.9-kg reduction in body fat. Two additional servings of yogurt were used to increase the dietary calcium intake in the experimental group compared with the control group.

Research has been conducted to determine the mechanism responsible for the “anti-obesity” effect of dietary calcium. Animal studies first studied the *agouti* obesity gene found in human adipocytes. The agouti protein stimulates the influx of calcium into adipocytes, thereby stimulating fatty acid synthase, an enzyme involved in lipogenesis that inhibits basal and agonist-stimulated lipolysis in human and murine adipocytes via a calcium-dependent mechanism.¹⁰⁰ Exogenous high calcium intake suppresses 1,25-(OH)₂-D and decreases calcium influx to the adipocyte (Figure 1). Increasing adipocyte intracellular calcium promotes triglyceride storage and exerts control over lipogenesis and inhibits lipolysis. The inhibitory effect of intracellular calcium is also believed to be partially responsible for the inhibition of phosphodiesterase.¹⁰³ Transgenic mice expressing agouti in adipose tissue were placed on low- and high-calcium diets, with the former exhibiting increases in lipogenesis, inhibition of lipolysis, and accelerated increases in body weight and fat mass.¹⁷ In the same mouse model, another experiment added a caloric restriction component in addition to calcium to determine whether additional fat loss could be created secondary to caloric restriction. As hypothesized, the low-calcium treatment

caused a two-fold increase in adipocyte intracellular calcium, a weight gain of 29%, and increase in pad fat mass, while the high-calcium treatments showed a 50% decrease in intracellular calcium and greater decreases in weight loss and fat pad mass. Fatty acid synthase was reduced significantly by a high calcium intake, with almost a two-fold change when the calcium was derived from dairy. Other animal studies confirm the positive effect of calcium on fat and weight reduction,¹⁰⁴ and suggest that rats on caloric restriction and restricted calcium intake have an increased bone turnover and decrease in BMD.¹⁰⁵

Human clinical trials have been conducted to assess the effect of calcium on weight loss and body composition during caloric restriction. In a study conducted by Zemel et. al,¹⁰⁶ subjects were randomized for 24 weeks to: 1) placebo pill with ≤ 1 servings of dairy per day totaling 400 to 500 mg of calcium, 2) high calcium using a control diet with an 800-mg calcium supplement, or 3) high dairy with 3 to 4 servings per day of lowfat dairy for a total calcium intake of 1200 to 1300 mg per day. All groups had a balanced deficit diet (–500 kcals). All groups lost weight, with the control losing 6.4 ± 2.5% of body weight, which was increased by 26% in the high-calcium group, and 70% in the high-dairy group. Fat loss as assessed by dual-energy X-ray absorptiometry followed a similar trend.

A similar study⁹³ included subjects randomized to diets similar to the Zemel study, specifically: 1) placebo pill with ≤ 500 mg calcium from either non-dairy or ≤ 1 servings of dairy per day, 2) high calcium using control diet with a 900-mg calcium supplement, or 3) high dairy with ≥3 lowfat dairy servings for a total daily calcium intake of 1200 to 1300 per day. All groups had a balanced deficit diet (–500 kcals). All groups lost weight, with the control losing 2.82 ± 2.76 kg of body weight, the high-calcium group losing 2.83 ± 2.8 kg, and the high-dairy group losing 4.20 ± 3.8 kg. Fat loss, as assessed by dual-energy X-ray absorptiometry, was significant for the high-dairy group (*p* < 0.05).

A randomized, 2-year exercise intervention in young, normal-weight women performed secondary analysis to assess any impact of exercise on calcium intake and body weight and body composition.¹⁰⁷ For all groups pooled together, regression analysis indicated a negative relationship between calcium intake and total body weight and body fat when adjusted for energy intake. Average intake was 781 ± 212 mg/d of calcium.

The above animal and human studies support a potential beneficial role for calcium on weight loss and body composition, with the benefit appearing greatest with dairy products. Zemel¹⁷ suggests that one of the additional components responsible for dairy’s increased effect is found in the whey fraction of milk. To examine

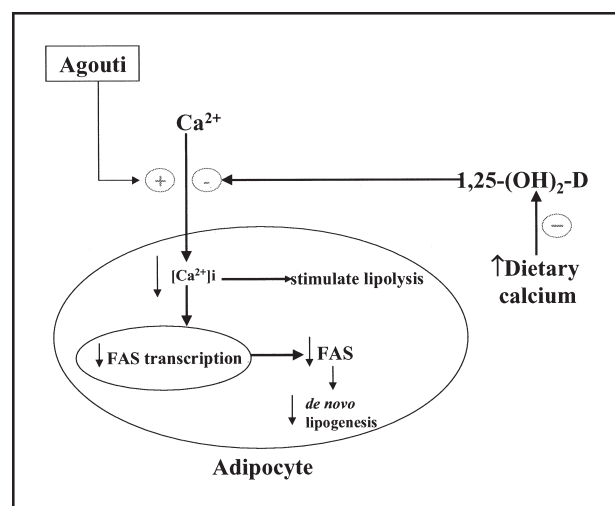


Figure 1. [Ca²⁺]-mediated mechanisms and regulation of adiposity. Figure modified and adapted with permission from Zemel MB, unpublished data. FAS = Fatty acid synthase.

the results of these calcium and dairy food studies on body composition and weight loss, Barr¹⁰⁸ performed a Medline search of all randomized studies using calcium or dairy that had data on change in body composition or weight. Nine studies were found using dairy; seven of these showed no significant differences in body weight or composition between control and treatment groups. Two other studies showed a significantly greater increase in weight for the dairy-supplemented group versus controls. The author notes that these results were in conflict with calcium eliciting increased energy utilization, but the results may be compromised if the subjects compensated in some way for the additional calories from the dairy supplements. Seventeen other studies using calcium supplements also showed no significant differences between calcium-supplemented and control groups, except for one study, which actually showed greater weight loss in the calcium-supplemented group. These studies did not include caloric restriction and did not have body weight or composition as the primary end points. Teegarden and Zemel¹⁰⁹ note that in order for an effect of calcium to be seen, caloric intake must be factored in. Additionally, most of the trials included normal-weight individuals in whom caloric restriction would not be appropriate. However, a pooled analysis of three caloric restriction studies investigating calcium supplementation and weight loss or body fat found no significant difference between placebo and calcium-supplemented groups (1 g/d calcium) of pre- and postmenopausal women.¹¹⁰

Clearly, more research is needed to assess calcium's impact on body composition and weight during caloric restriction and to determine if dairy calcium exerts an additional positive effect above that of calcium supplementation.

Other Potential Influences on Loss of Bone During Caloric Restriction

The mechanism responsible for the loss of bone mass during weight loss is unclear. A number of possible reasons have been explored. Jensen et al.⁵⁰ and others have suggested that the bone loss associated with weight loss may be due to the decrease in weight applied to bone, e.g. mechanical load, which influences bone remodeling. If this is the case, then the effect of weight loss should be greater on weight-bearing bones than on non-weight-bearing bones.¹⁹ Anderson et al.¹¹¹ examined this hypothesis to see if exercise could preserve the loss by adding a resistance training component to one of the diet groups, but no significant bone-sparing effect was observed. Svendsen et al.¹¹² found that decreases in lumbar spine BMD actually were greater in the diet and exercise group than in the diet-only group. In a 6-year prospective study in pre- and perimenopausal women, current physical activity was not correlated with BMD or bone

loss.¹¹³ However, Ryan et al.¹¹⁴ did find a benefit of exercise in preserving regional BMD.

McLean et al.¹¹⁵ looked at cognitive change among dieters and implicated the production of cortisol as a contributing factor to bone loss during weight loss. Leptin levels may also influence the rate of bone turnover and has been shown to decrease during weight loss.¹¹⁶ It has also been suggested that leptin regulates bone formation independent of its influence on body weight.¹¹⁷ Another factor could be a decrease in adipose cells resulting in a reduction in estrogen or estrone levels, as confirmed by Ricci et al.⁵⁶ Parathyroid hormone levels tend to be altered during weight loss and this slight increase may also be a contributor.^{56,118}

There have also been methodological issues raised when the analytical method used for determining bone loss is dual-energy x-ray absorptiometry.¹¹⁹⁻¹²² The increased thickness of soft tissue in obese subjects may interfere with bone edge detection and affect the accuracy of measurements.^{8,51} Measurements are also expressed in areal density as grams per centimeter squared, and do not factor in the dimension of depth.^{123,124} Obese subjects tend to have increased bone size, resulting in a possible overestimation of BMD. Another potential consideration may be that women with greater bone mass also lose it at a faster rate than women of lower bone mass.¹²⁵ Anderson et al.¹¹¹ noted that because bone mass is higher in obese women than in normal-weight women, the bone loss seen from weight loss only serves to bring those women back to within the "normal" range.

Many individuals undergo repeated episodes of caloric restriction, so the effect of weight cycling on bone mass and turnover has also been investigated. Results from these studies are not conclusive.^{60,96,126} Recently, however, Bacon et al.⁶⁰ examined a group of obese women, each with a history of chronic dieting, and found that one-third had either osteopenia or osteoporosis.

While other nutrients play a role in bone metabolism, most are within adequate intake levels compared with levels of calcium intake. However, it is unclear whether other nutrients are compromised during caloric restriction to the degree that calcium is, and this is of particular importance for individuals who engage in repeated weight loss episodes. Nutrients found in fruit and vegetables have been suggested as having a positive association with BMD for late premenopausal women.¹¹⁷ Vitamin D is needed for calcium absorption in the intestine and also plays a role in bone turnover.¹²⁷ Positive effects of calcium on bone have been reported both with and without the inclusion of vitamin D.¹²⁸ This may be explained partially because the major source of vitamin D is cutaneous production via sunlight exposure, which is geographically variable. Trials looking to differentiate the effect of vitamin D or calcium have shown

that the preservation of bone is due primarily to calcium and not to vitamin D,⁸⁴ although a deficiency of vitamin D could have negative consequences for bone metabolism.⁹⁶ Perhaps the largest contribution to bone loss during caloric restriction is due to a reduced calcium intake.

Specific dietary regimens have also been investigated. The DASH (Dietary Approaches to Stop Hypertension) diet was used during a 90-day randomized crossover trial in middle-aged, mostly overweight men and women. Markers of bone turnover were significantly reduced compared with control diets during secondary analysis.¹²⁹ A recent review looking at vegetarian-based diets and bone mass found no significant increase or decrease in bone mass in the nine studies investigated.¹³⁰

Considerations for Choices of Calcium Source

While available studies suggest preservation of bone with adequate calcium during caloric restriction, and that dairy sources of calcium may yield additional weight/fat loss during caloric restriction, there are other factors to consider between supplementation or dietary sources (Table 2). Those who try to reduce weight via caloric restriction commonly strive to consume less fat.^{17,131-132} Dairy products, a major source of dietary calcium, are sometimes perceived as fat-containing foods and are

typically not emphasized during periods of caloric restriction.¹³³⁻¹³⁶ As mentioned, this may have a deleterious effect on bone health for premenopausal women already striving to meet calcium intake recommendations.

Various issues have been raised surrounding the sources of calcium available. Supplements can be easier to take than dietary sources, less expensive, better absorbed, and can meet recommendations with one pill, as well as being more accepted by a sizable portion of the population who are lactose intolerant.¹³⁷⁻¹³⁹ Those who follow a strict plant-based diet might benefit from supplements,¹⁴⁰ particularly during weight loss. While many plant-based sources of calcium generally have good fractional absorption,¹⁴¹⁻¹⁴³ with some better than dairy sources,^{140,144} their intake alone falls short of meeting calcium requirements for the majority of the population. The challenge with plant sources is getting sufficient quantities of intake. Dairy products remain the most significant calcium source for the public.¹⁴⁵ The National Health Interview Survey in 1989 quantified calcium supplement use at roughly 25 percent for women.¹⁴⁶ Pill supplementation comes without the addition of cholesterol and saturated fats, known risk factors for cardiovascular disease, and has been shown to have some favorable effects on blood lipids but in general has no significant additional effect.¹⁴⁷

Dairy products, as a source of dietary calcium and other nutrients, have been proposed over supplements for additional reasons beyond their effect on bone health.¹⁴⁴ The CARDIA study indicated a reduction in cardiovascular and type 2 diabetes risk factors with increased dairy intake.¹⁴⁸ A recent prospective study found a modest reduction in risk of distal colorectal cancer with higher calcium intake.¹⁴⁹ Others note reductions in hypertension and homocysteine levels in diets such as DASH, which contain lowfat dairy.¹⁵⁰ Other components of dairy, such as conjugated linoleic acid, have been suggested to be potentially protective of certain diseases and have exhibited antitumor properties,^{151,152} although one epidemiological study found conjugated linoleic acid intake to have a weak but positive relation with breast cancer incidence.¹⁵³ Other forms of cancer have been associated with dairy consumption,^{154,155} but many studies have had conflicting results, with some showing dairy consumption to be protective and others indicating a lack of protective effect.^{145,156-159} Other studies and one review have suggested that dairy consumption can be related to an elevated insulinemic index.¹⁶⁰⁻¹⁶² While dairy products contain cholesterol and saturated fats, studies did not find significant increases with dairy consumption, but rather decreases in plasma lipid and lipoproteins related to cardiovascular risk.¹⁴⁷ However, in hypercholesterolemic individuals who had been on a lipid-lowering

Table 2. Characteristics of Calcium Sources

Source	Characteristics
Supplements	Positive: Less expensive Slightly better absorbed than dairy Can meet recommendation with one or two pills Good for lactose-intolerant people Negative: Increased risk of kidney stones
Dairy	Positive: Additional benefit of fat loss during caloric restriction Contains other vitamins and minerals Negative: Sometimes perceived as high fat and avoided High in cholesterol and saturated fat Mixed results regarding effect on chronic diseases
Plant-based	Positive: Excellent fractional absorption Contains vitamins, minerals, and other phytonutrients Negative: Challenging to meet recommendations with just plant-based sources

diet, the addition of dairy for 6 weeks increased LDL and decreased HDL, while also increasing lipid peroxidation.¹⁶³

Dietary sources of calcium have been shown to decrease the risk of kidney stones, while supplemental calcium has been shown to increase risk and could possibly interfere with other minerals.^{85,164} Lastly, some follow-up studies have shown that the positive effects of calcium did not persist years later for pill supplements⁸⁵ and dairy calcium,¹⁶⁵ although one study suggested that the effects did persist with dairy.¹⁶⁶

Regardless of the choice of calcium sources, the most important factor is to choose one as a source or addition to one's total calcium intake, particularly during caloric restriction.

Conclusions and Applications

It is prudent to suggest that weight loss during premenopausal years is desirable and outweighs the potential risks to bone health that are now being investigated. The effects on bone metabolism during this time may impact bone health in the future, when bone preservation is of the utmost importance to minimize osteoporotic-related fractures. Available premenopausal studies show a decline in bone mass with weight loss and low calcium intakes. However, there are still many unknowns relative to the cause of bone loss during weight loss. Findings from studies examining bone health during weight loss suggest that high calcium intake during energy restriction may attenuate the loss of bone. Intake levels for calcium during caloric restriction studies range from 1000 to 1800 mg/d. As most women's calcium intake is well below this recommendation, adding an additional 500 to 1000 mg/d from dietary or supplemental sources would not exceed the upper intake level and could provide a benefit to bone metabolism, weight loss, and fat loss during caloric restriction. The influence of high calcium intake beyond standard recommendations warrants additional investigation for additional weight loss, fat loss, and preservation of bone mass. If supplements are recommended, the addition of vitamin D is suggested. At this time, unless there is a known medical condition or heredity history, dual-energy X-ray absorptiometry scans to assess bone status are not performed in premenopausal women, but could be beneficial in identifying women at risk for future osteoporotic disease.

For many women, the stage appears set for possible future osteoporotic disease due to a combination of already low calcium intake, normal bone loss due to aging, the negative influence of weight loss on bone mass, and potentially an additional insult from weight cycling. All of these together represent a risk to bone health and may predispose premenopausal women to future osteoporotic events. Because calcium intake and

weight loss appear to affect bone mass, it is important for additional studies to determine the risks and benefits of both concurrently. Longer-term studies are needed to evaluate whether the influence of calcium persists during and after weight loss, and also to evaluate other potential influences on bone loss in order to ascertain adequate calcium intake levels.

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